

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 08 FEB 2006

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Applicant's or agent's file reference GHS/P504207WO		FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/GB2004/004388		International filing date (day/month/year) 15.10.2004		Priority date (day/month/year) 30.10.2003
International Patent Classification (IPC) or national classification and IPC C07D207/26				
Applicant DAVY PROCESS TECHNOLOGY LIMITED				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau a total of 2 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 30.08.2005		Date of completion of this report 07.02.2006		
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized Officer De Jong, B Telephone No. +31 70 340-2833		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/GB2004/004388

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1, 2, 4-10	as originally filed
3	filed with telefax on 30.08.2005

Claims, Numbers

7-32	as originally filed
1-6	filed with telefax on 30.08.2005

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/GB2004/004388

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-32
	No: Claims	
Inventive step (IS)	Yes: Claims	1-32
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-32
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Reference is made to the following document:

D3: WO 02/102772 A (BATTELLE) 27 December 2002

Novelty

The prior art does not disclose the preparation of a lactam using a homogeneous ruthenium or osmium catalyst with a phosphine ligand.

Inventive step

The document D3, which is regarded as being the closest prior art, discloses the preparation of a lactam using a heterogeneous metal catalyst which comprises carbon, metal oxide and a metal selected from Pd, R, Pt, Ru, Ni and Co. These catalysts do not have a phosphine ligand and there is no example in D3 in which a ruthenium catalyst is used. Furthermore the process in D3 has at least 3 steps (see page 3, line 21). In one of these steps the imide of formula A is extracted into an organic solvent.

The process according to the present application is therefore not obvious from the teaching of D3.

Citation of the prior art

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D3 is not mentioned in the description, nor is this document identified therein.

4931573 where reactions are carried out in the presence of an organic solvent and a metal selected from Group IVA, VA and III is required as a promotor.

Another example of the use of a promotor may be found in US 5077442. In this case a phosphorous compound is used to promote selectivity and conversion. This document teaches that any water produced in the reaction is removed from the reaction zone as the presence of water is said to decrease selectivity and conversion.

Another suitable promotor described is a conjugate base of an acid and in this connection reference may be made back to US 5021589 and US 4892955. In this latter case, it is noted that components of the catalyst system are susceptible to hydrolysis under the reaction conditions and that a hydrogen purge was required to remove water produced during the reaction.

In view of the foregoing it will be understood that there is still a need for a process for the production of lactams in a cost-effective manner from readily available starting materials. This can be achieved by the homogeneous hydrogenation of dicarboxylic acids and derivatives thereof with the appropriate amine using a ruthenium/phosphine catalyst system in the presence of water. Surprisingly, despite the teachings of the prior art, it has been established that the presence of water is not only not disadvantageous but indeed offers positive advantages.

Thus according to the present invention there is provided a homogeneous process for the hydrogenation of dicarboxylic acid and/or derivative thereof with amine in the presence of a catalyst comprising:

- (a) ruthenium or osmium; and
- (b) an organic phosphine;

and wherein the hydrogenation is carried out in the presence of water

and wherein the product of the process is a lactam

By "homogeneous process" we mean that the catalyst is dissolved in the solvent for the reaction and that at least some of the water present and at least some of the reactants must be in phase

Claims

1. A homogeneous process for the hydrogenation of dicarboxylic acid and/or derivative thereof with an amine in the presence of a catalyst comprising:
 - (a) ruthenium or osmium; and
 - (b) an organic phosphine;and wherein the hydrogenation is carried out in the presence of water
and wherein the product of the process is a lactam
2. A homogeneous process according to Claim 1 wherein the water is present in at least 1% by weight.
3. A homogeneous process according to Claim 1 or 2 wherein the dicarboxylic acid and/or derivative thereof is selected from one or more of dicarboxylic acids, polycarboxylic acids, anhydrides, monoesters or diesters of dicarboxylic acids, monoamides or diamides of dicarboxylic acids, salts, such as amine salts, of dicarboxylic acids or mixtures thereof.
4. A homogeneous process according to any one of Claims 1 to 3 wherein the dicarboxylic acid and/or derivative thereof is a C_4 to C_{12} dicarboxylic acid.
5. A homogeneous process according to any one of Claims 1 to 4 wherein the dicarboxylic acid and/or derivative thereof is saturated or unsaturated.
6. A homogeneous process according to any one of Claims 1 to 5 wherein the dicarboxylic acid and/or derivative thereof is selected from maleic acid, fumaric acid, succinic acid, maleic anhydride, adipic acid, and succinic anhydride.